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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/634,252	08/07/2000	Douglas P. Cerretti	03260.0051	3642

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	**PAPER NUMBER**
1652	18

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/634,252	CERRETTI, DOUGLAS P.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,21-23,30-32,34-36,38,40,42 and 44-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *15,16,21-23,30-32,38,40,42 and 44-49* is/are allowed.

6)☒ Claim(s) *34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

Applicant's Amendment C, Paper No. 16 filed March 11, 2003, has been entered. The cancellation of claims 33, 37, 39, 41, and 43, the amendments to claims 15, 31, 32, 34, 35, 38 and 40, and Applicant's arguments at page 7 of Paper No. 16 pointing out the inappropriate citation of Sheppard et al.('199) as prior art, overcome all of the objections to, and rejections of record of, claims 15, 16, 21-23, 30-32, 38, 40, 42, 44, 45 and 46. Claims 47-49 newly-submitted with Paper No. 16 are likewise free of the objections and rejections of record, thus claims 15, 16, 21-23, 30-32, 38, 40, 42 and 44-49 are indicated as allowable herein. The rejections of record of claims 34-36 under 35 U.S.C. §§101 and 112, first paragraph, for lack utility, lack of enablement as to use and as to making, and for lack of an adequate written description in the specification are, however, maintained.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34 and 35 remain rejected, essentially for reasons of record, under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

Applicant's arguments filed March 11, 2003, have been fully considered but they are not persuasive with respect to the amended claims 34 and 35 which permit a polypeptide encoded by a claimed polynucleotide to differ by, respectively, 21 and 10 amino acids from the disclosed amino acid sequence of 104 amino acids between positions 496 and 599 of SEQ ID NO:4, inclusive, thus failing to support the utility argued by Applicant where the nature of the numerous changes permitted in these large polypeptide genera cannot be predictably determined to sustain a recited disintegrin activity. A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility. While a

recited utility - disintegrin activity - is substantial, there are no specific locations indicated, either in the claims or in the specification, where any amino acid substitutions, deletions, or additions can be made, or from which such are changes are excluded, thus the preservation of a recited disintegrin activity is not credible. Thus the specification provides no specific *in vitro* utility that is also credible for a nucleic acid encoding an undisclosed variant of the polypeptide region between positions 496 and 599. A method of use of a material for further research to determine, e.g., whether or not it can retain the recited biological activity, thus confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). Nothing in the specification indicates that Applicant knew of any specific variant having the recited utility and encoded by a nucleic acid sequence when the application was filed. The rejection of record is therefore sustained but may be overcome by canceling the rejected claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34 and 35 also remain rejected for reasons of record under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The rejection of record is therefore sustained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-36 remain rejected, essentially for reasons of record, under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed March 11, 2003, have been fully considered but they are not persuasive with respect to the amended claims 34-36 which permit a polypeptide encoded by a polynucleotide of claims 34 and 35 to differ by, respectively, 21 and 10 amino acids from the disclosed amino acid sequence of 104 amino acids between positions 496 and 599 of SEQ ID NO:4, inclusive, or permit a polypeptide encoded by a polynucleotide of claim 36 to differ from the amino acid sequence of 104 amino acids present between positions 496 and 599 of SEQ ID NO:4 at the 17 amino acid positions outside the regions defined by positions 499 through 530 and 532 through 586. No specific modifications are disclosed or suggested in the specification that will give rise to specific members of the genera of claimed molecules, differing significantly in their coding capacity from that of SEQ ID NO:2 for the amino acid sequence of SEQ ID NO:4 between positions 496 and 599. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The Court of Appeals for the Federal Circuit has also held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Like the claims invalidated by the appellate panel in *University of California v. Eli Lilly*, claims 34-35 rejected herein remain designed to embrace other, as yet unknown,

human metalloprotease-disintegrins and metalloprotease-disintegrins of other mammalian species. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of a nucleic acid sequence encoding any of these undisclosed generic domains to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). Because the specification fails to exemplify or describe the design or preparation of the subject matters of such variant nucleic acid sequences encoding polypeptides that diverge regionally from the amino acid sequence of SEQ ID NO:4, nor indicate where the region of SEQ ID NO:4 between positions 496 and 599 might diverge, nor how it might diverge, the rejection of record is therefore sustained, but may be overcome by canceling the rejected claims.

Claims 34-36 remain rejected, essentially for reasons of record, under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for preparation of nucleic acid sequences encoding a metalloprotease-disintegrin of SEQ ID NO:4, as well as nucleic acid sequences encoding fragments of SEQ ID NO:4 having disintegrin activity, does not reasonably provide enablement for preparation of nucleic acid sequences encoding a polypeptide having an amino acid sequence that diverges, by virtue of amino acid substitutions, deletions and insertions, or combinations thereof at as many as 20%, or even 10%, of the amino acid positions between positions 496 and 599 of the amino acid sequence of SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed March 11, 2003, have been fully considered but they are not persuasive with respect to the amended claims 34-36 whereby a polypeptide encoded by a polynucleotide of claims 34 and 35 may differ by, respectively, 21 and 10 amino acids from the disclosed amino acid sequence of 104 amino acids between positions 496 and 599 of SEQ ID NO:4, inclusive, yet somehow retain disintegrin activity, or whereby a polypeptide encoded by a polynucleotide of claim 36 may differ from the amino acid sequence of 104 amino acids present between positions 496 and 599 of SEQ ID NO:4 at

the 17 amino acid positions outside the regions defined by positions 499 through 530 and 532 through 586, yet retain the excluded regions in a proper orientation for disintegrin activity. Applicant suggests at page 5 of Paper No. 16 that the publication of Jia et al., submitted by Applicant with Paper No. 12 filed August 22, 2002, and now made of record herein with the accompanying PTO-Form 892, supports any and all modifications embraced by claims 34-36. Yet Jia et al. establish only, see Table 1 at page 13100, that conserved cysteines contributing to disulfide bonds are best retained in disintegrin domains, that negatively-charged amino acids adjacent to conserved cysteines are best retained, but that an "RGDA" motif may be imported into one conserved cysteine site in one disintegrin domain of the diamondback rattlesnake venom metalloprotease toxin to replace the tetrapeptide "RSEC". Applicant's recited genera far exceed the few modifications made by Jia et al. and mere sequence perturbation will not enable the design and preparation of nucleotide sequences encoding a myriad of divergent disintegrin domains derived from the region of SEQ ID NO:4 recited in claims 34-36 and provide the public with a nucleotide sequence encoding a disintegrin domain that retains its native function. The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The Federal Circuit approved this standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). The rejection of record is therefore sustained.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at 703.308.3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct fax phone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
May 23, 2003

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